

WHAT IS CLAIMED IS:

1. A method for producing an immune response in a subject comprising the steps of:

- 5
- (a) administering to the subject a vaccine composition comprising a component against which an immune response is desired to be induced; and
- (b) administering to the subject a heat shock protein preparation, wherein the heat shock protein preparation does not display the immunogenicity of the component;
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such that an immune response to the component is produced in the subject.

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2. A method of inducing an immune response by a vaccine composition in a subject comprising the steps of:

- (a) administering to the subject a heat shock protein preparation; and
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- (b) administering to the subject a vaccine composition comprising a component against which an immune response is desired to be induced, the vaccine composition being in an amount that is sub-immunogenic for the component in the absence of step(a),
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such that an immune response to the component is induced in the subject, and wherein the heat shock protein preparation does not display the immunogenicity of the component.

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3. A method of treating or preventing an infectious disease in a subject comprising the steps of:

- (a) administering to the subject a vaccine composition comprising a component that displays the antigenicity of an infectious agent that causes the infectious disease; and
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(b) administering to the subject an amount of a heat shock protein preparation effective in combination with step (a) to induce or increase an immune response to the component in the subject, wherein the heat shock protein preparation does not display the immunogenicity of the component.

4. A method of treating or preventing a cancer in a subject comprising the steps of:

- (a) administering to the subject a vaccine composition comprising a component that displays the antigenicity of a cancer cell; and
- (b) administering to the subject an amount of a heat shock protein preparation effective to induce or increase an immune response in the subject to the component, wherein the heat shock protein preparation does not display the immunogenicity of the component.

5. The method of claim 1, wherein the immune response to the component produced in the subject is increased relative to the immune response to the component in the subject in the absence of step (b).

6. The method according to claim 1 wherein the heat shock protein preparation comprises a heat shock protein selected from the group consisting of hsp70, hsp90, gp96, calreticulin, and a combination thereof.

7. The method according to claim 2 wherein the heat shock protein preparation comprises a heat shock protein selected group consisting of hsp70, hsp90, gp96, calreticulin, and a combination thereof.

8. The method according to claim 3 wherein the heat shock protein preparation comprises a heat shock protein selected from the group consisting of hsp70, hsp90, gp96, calreticulin, and a combination thereof.

5 9. The method according to claim 4 wherein the heat shock protein preparation comprises a heat shock protein selected from the group consisting of hsp70, hsp90, gp96, calreticulin, and a combination thereof.

10 10. The method according to claim 1 wherein the heat shock protein preparation comprises heat shock protein-peptide complexes.

15 11. The method according to claim 2 wherein the heat shock protein preparation comprises heat shock protein-peptide complexes.

20 12. The method according to claim 3 wherein the heat shock protein preparation comprises heat shock protein-peptide complexes.

25 13. The method according to claim 4 wherein the heat shock protein preparation comprises heat shock protein-peptide complexes.

30 14. The method according to claim 1 wherein the heat shock protein preparation comprises purified heat shock proteins.

35 15. The method according to claim 2 wherein the heat shock protein preparation comprises purified heat shock proteins.

16. The method according to claim 3 wherein the heat shock protein preparation comprises purified heat shock proteins.

Sub B3  
17. The method according to claim 4 wherein the heat shock protein preparation comprises purified heat shock proteins.

5 18. The method according to claim 1 wherein the heat shock protein preparation comprises heat shock protein-peptide complexes and purified heat shock proteins.

10 19. The method according to claim 2 wherein the heat shock protein preparation comprises heat shock protein-peptide complexes and purified heat shock proteins.

15 20. The method according to claim 3 wherein the heat shock protein preparation comprises heat shock protein-peptide complexes and purified heat shock proteins.

Sub B4  
21. The method according to claim 4 wherein the heat shock protein preparation comprises heat shock protein-peptide complexes and purified heat shock proteins.

20 22. The method according to claim 1 wherein the subject is human and the heat shock protein preparation comprises mammalian heat shock proteins.

25 23. The method according to claim 2 wherein the subject is human and the heat shock protein preparation comprises mammalian heat shock proteins.

30 24. The method according to claim 3 wherein the subject is human and the heat shock protein preparation comprises mammalian heat shock proteins.

Sub B5  
35 25. The method according to claim 4 wherein the subject is human and the heat shock protein preparation comprises mammalian heat shock proteins.

26. The method according to claim 1, 2, 3, or 4 wherein the heat shock protein is administered before the administration of the vaccine composition.

27. The method according to claim 1, 2, 3, or 4 wherein the heat shock protein preparation is administered concurrently with the administration of the vaccine composition.

5 28. The method according to claim 1, 2, 3, or 4 wherein the heat shock protein is preparation administered after the administration of the vaccine composition.

10 29. The method according to claim 6, 7, 8, or 9 wherein the heat shock protein preparation is administered before the administration of the vaccine composition.

15 30. The method according to claim 6, 7, 8, or 9 wherein the heat shock protein preparation is administered concurrently with the administration of the vaccine composition.

20 31. The method according to claim 6, 7, 8, or 9 wherein the heat shock protein is administered after the administration of the vaccine composition.

32. The method according to claim 10, 11, 12, or 13 wherein the heat shock protein is administered before the administration of the vaccine composition.

25 33. The method according to claim 10, 11, 12, or 13 wherein the heat shock protein is administered concurrently with the administration of the vaccine composition.

30 34. The method according to claim 10, 11, 12, or 13 wherein the heat shock protein is administered after the administration of the vaccine composition.

35 35. The method according to claim 14, 15, 16, or 17 wherein the heat shock protein is administered before the administration of the vaccine composition.

36. The method according to claim 14, 15, 16, or 17 wherein the heat shock protein is administered concurrently with the administration of the vaccine composition.

5 37. The method according to claim 14, 15, 16, or 17 wherein the heat shock protein is administered after the administration of the vaccine composition.

10 38. The method according to claim 18, 19, 20, or 21 wherein the heat shock protein preparation is administered before the administration of the vaccine composition.

15 39. The method according to claim 18, 19, 20, or 21 wherein the heat shock protein preparation is administered concurrently with the administration of the vaccine composition.

20 40. The method according to claim 18, 19, 20, or 21 wherein the heat shock protein is administered after the administration of the vaccine composition.

25 41. The method according to claim 18, 19, 20, or 21 wherein the heat shock protein preparation and the vaccine composition are both administered on the same day.

30 42. The method of claim 1, 2, 3, 4, 5, 22, 23, 24, or 25 wherein the vaccine composition is a live vaccine, an attenuated vaccine, a subunit vaccine, a DNA vaccine, or a RNA vaccine.

35 43. The method according to claim 3 wherein the infectious disease is selected from the group consisting of hepatitis A virus, hepatitis B virus, hepatitis C virus, influenza, varicella, adenovirus, herpes simplex I virus, herpes simplex II virus, cholera, rhinovirus, ECHO virus, rotavirus, respiratory syncytial virus, papilloma virus, papova virus, cytomegalovirus, echinovirus, arbovirus,

hantavirus, coxsackie virus, mumps virus, measles virus, rubella virus, polio virus, human immunodeficiency virus type I (HIV-I), human immunodeficiency virus type II (HIV-II), mycobacteria, rickettsia, mycoplasma, neisseria, legionella, leishmania, kokzidioa, trypanosoma and chlamydia.

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44. The method according to claim 4 wherein the cancer is selected from the group consisting of fibrosarcoma, myxosarcoma, liposarcoma, chondrosarcoma, osteogenic sarcoma, chordoma, angiosarcoma, endotheliosarcoma, lymphangiosarcoma, lymphangioendotheliosarcoma, synovioma, mesothelioma, Ewing's tumor, leiomyosarcoma, rhabdomyosarcoma, colon carcinoma, pancreatic cancer, breast cancer, ovarian cancer, prostate cancer, squamous cell carcinoma, basal cell carcinoma, adenocarcinoma, sweat gland carcinoma, sebaceous gland carcinoma, papillary carcinoma, papillary adenocarcinomas, cystadenocarcinoma, medullary carcinoma, bronchogenic carcinoma, renal cell carcinoma, hepatoma, bile duct carcinoma, choriocarcinoma, seminoma, embryonal carcinoma, Wilms' tumor, cervical cancer, testicular tumor, lung carcinoma, small cell lung carcinoma, bladder carcinoma, epithelial carcinoma, glioma, astrocytoma, medulloblastoma, craniopharyngioma, ependymoma, pinealoma, hemangioblastoma, acoustic neuroma, oligodendroglioma, meningioma, melanoma, neuroblastoma, retinoblastoma; leukemias, e.g., acute lymphocytic leukemia and acute myelocytic leukemia (myeloblastic, promyelocytic, myelomonocytic, monocytic and erythroleukemia); chronic leukemia (chronic myelocytic (granulocytic) leukemia and chronic lymphocytic leukemia); and polycythemia vera, lymphoma (Hodgkin's disease and non-Hodgkin's disease), multiple myeloma, Waldenström's macroglobulinemia, and heavy chain disease.

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45. The method of claim 3, wherein the method is for preventing an infectious disease.

46. The method of claim 4, wherein the method is for treating a cancer.

47. The method of claim 4, wherein the method is for preventing a cancer.

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48. A kit comprising:

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(a) a first container containing a heat shock protein preparation in an amount effective to increase an immune response elicited by a vaccine composition against a component of the vaccine composition against which an immune response is desired; and

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(b) a second container containing the vaccine composition in an amount that, when administered before, concurrently with, or after the administration of the heat shock protein preparation of (a), is effective to induce an immune response against the component.

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49. The kit according to claim 48 wherein the heat shock protein preparation comprises a heat shock protein selected from the group consisting of hsp70, hsp90, gp96, calreticulin, and a combination thereof.

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50. The kit according to claim 48 wherein the heat shock protein preparation comprises heat shock protein-peptide complexes.

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51. The kit according to claim 48 wherein the heat shock protein preparation comprises purified heat shock proteins.

52. The kit according to claim 48 wherein the heat shock protein preparation comprises heat shock protein-peptide complexes and purified heat shock proteins.



53. The kit according to claim 48 wherein the heat shock protein preparation comprises mammalian heat shock proteins.

54. The kit according to claim 48 wherein the amount of vaccine composition in the second container is insufficient for inducing an immune response in a subject in the absence of administering the heat shock protein preparation in the first container.

55. A method for producing an immune response in a subject comprising the steps of:

- (a) administering to the subject a vaccine composition comprising a component against which an immune response is desired to be induced; and
  - (b) administering to the subject a composition comprising activated antigen presenting cells, wherein the antigen presenting cells have been contacted with a heat shock protein preparation, and wherein the heat shock protein preparation does not display the immunogenicity of the component;
- such that an immune response to the component is produced in the subject.

56. A method of inducing an immune response by a vaccine composition in a subject comprising the steps of:

- (a) administering to the subject a composition comprising activated antigen presenting cells, wherein the antigen presenting cells have been activated by contacting the antigen presenting cells with a heat shock protein preparation; and
- (b) administering to the subject a vaccine composition comprising a component against which an immune response is

desired to be induced, the vaccine composition being in an amount that is sub-immunogenic for the component in the absence of step(a),

such that an immune response to the component is induced in the subject, and wherein the heat shock protein preparation does not display the immunogenicity of the component.

57. A method of treating or preventing an infectious disease in a subject comprising the steps of:

- (a) administering to the subject a vaccine composition comprising a component that displays the antigenicity of an infectious agent that causes the infectious disease; and
- (b) administering to the subject an amount of a composition comprising activated antigen presenting cells, wherein the antigen presenting cells have been activated by contacting the antigen presenting cells with a heat shock protein preparation, and wherein the amount of the composition comprising the activated antigen presenting cells is effective in combination with step (a) to induce or increase an immune response to the component in the subject, and wherein the heat shock protein preparation does not display the immunogenicity of the component.

58. A method of treating or preventing a cancer in a subject comprising the steps of:

- (a) administering to the subject a vaccine composition comprising a component that displays the antigenicity of a cancer cell; and
- (b) administering to the subject an amount of a composition comprising activated

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antigen presenting cells, wherein the antigen presenting cells have been activated by contacting the antigen presenting cells with a heat shock protein preparation, and wherein the amount of the composition comprising the activated antigen presenting cells is effective in combination with step (a) to induce or increase an immune response to the component in the subject, and wherein the heat shock protein preparation does not display the immunogenicity of the component.

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59. The method according to claim 55 wherein the heat shock protein preparation comprises a heat shock protein selected from the group consisting of hsp70, hsp90, gp96, calreticulin, and a combination thereof.

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60. The method according to claim 56 wherein the heat shock protein preparation comprises a heat shock protein selected group consisting of hsp70, hsp90, gp96, calreticulin, and a combination thereof.

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61. The method according to claim 57 wherein the heat shock protein preparation comprises a heat shock protein selected from the group consisting of hsp70, hsp90, gp96, calreticulin, and a combination thereof.

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62. The method according to claim 58 wherein the heat shock protein preparation comprises a heat shock protein selected from the group consisting of hsp70, hsp90, gp96, calreticulin, and a combination thereof.

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63. The method according to claim 55 wherein the subject is human and the heat shock protein preparation comprises mammalian heat shock proteins.

64. The method according to claim 56 wherein the subject is human and the heat shock protein preparation comprises mammalian heat shock proteins.

5 65. The method according to claim 57 wherein the subject is human and the heat shock protein preparation comprises mammalian heat shock proteins.

10 66. The method according to claim 58 wherein the subject is human and the heat shock protein preparation comprises mammalian heat shock proteins.

15 67. The method according to claim 55, 56, 57, or 58 wherein the activated antigen presenting cells are administered before the administration of the vaccine composition.

20 68. The method according to claim 55, 56, 57, or 58 wherein the activated antigen presenting cells are administered concurrently with the administration of the vaccine composition.

25 69. The method according to claim 55, 56, 57, or 58 wherein the activated antigen presenting cells are administered after the administration of the vaccine composition.

30 70. The method of claim 55, 56, 57, or 58 wherein the vaccine composition is a live vaccine, an attenuated vaccine, a subunit vaccine, a DNA vaccine, or a RNA vaccine.

35 71. The method according to claim 57 wherein the infectious disease is selected from the group consisting of hepatitis A virus, hepatitis B virus, hepatitis C virus, influenza, varicella, adenovirus, herpes simplex I virus, herpes simplex II virus, rinderpest, rhinovirus, echovirus, rotavirus, respiratory syncytial virus, papilloma virus, papova virus, cytomegalovirus, echinovirus, arbovirus, hantavirus, coxsackie virus, mumps virus, measles virus,

rubella virus, polio virus, human immunodeficiency virus type I (HIV-I), human immunodeficiency virus type II (HIV-II), mycobacteria, rickettsia, mycoplasma, neisseria, legionella, leishmania, kokzidioa, trypanosoma and chlamydia.

5                   72. The method according to claim 58 wherein the cancer is selected from the group consisting of  
fibrosarcoma, myxosarcoma, liposarcoma, chondrosarcoma,  
osteogenic sarcoma, chordoma, angiosarcoma,  
10 endotheliosarcoma, lymphangiosarcoma,  
lymphangioendotheliosarcoma, synovioma, mesothelioma,  
Ewing's tumor, leiomyosarcoma, rhabdomyosarcoma, colon  
carcinoma, pancreatic cancer, breast cancer, ovarian cancer,  
prostate cancer, squamous cell carcinoma, basal cell  
15 carcinoma, adenocarcinoma, sweat gland carcinoma, sebaceous  
gland carcinoma, papillary carcinoma, papillary  
adenocarcinomas, cystadenocarcinoma, medullary carcinoma,  
bronchogenic carcinoma, renal cell carcinoma, hepatoma, bile  
duct carcinoma, choriocarcinoma, seminoma, embryonal  
20 carcinoma, Wilms' tumor, cervical cancer, testicular tumor,  
lung carcinoma, small cell lung carcinoma, bladder  
carcinoma, epithelial carcinoma, glioma, astrocytoma,  
medulloblastoma, craniopharyngioma, ependymoma, pinealoma,  
hemangioblastoma, acoustic neuroma, oligodendroglioma,  
25 meningioma, melanoma, neuroblastoma, retinoblastoma;  
leukemias, e.g., acute lymphocytic leukemia and acute  
myelocytic leukemia (myeloblastic, promyelocytic,  
myelomonocytic, monocytic and erythroleukemia); chronic  
leukemia (chronic myelocytic (granulocytic) leukemia and  
30 chronic lymphocytic leukemia); and polycythemia vera,  
lymphoma (Hodgkin's disease and non-Hodgkin's disease),  
multiple myeloma, Waldenström's macroglobulinemia, and heavy  
chain disease.

35                   73. A method for producing an immune response in  
a subject comprising the steps of:

- (a) administering to the subject a vaccine composition comprising a component

against which an immune response is desired to be induced;

- (b) administering to the subject a first heat shock protein preparation, wherein the first heat shock protein preparation does not display the immunogenicity of the component; and
- (c) administering to the subject an amount of a composition comprising activated antigen presenting cells, wherein the antigen presenting cells have been activated by contacting the antigen presenting cells with a second heat shock protein preparation which does not display the immunogenicity of the component;

such that an immune response to the component is produced in the subject.

74. A method of inducing an immune response by a vaccine composition in a subject comprising the steps of:

- (a) administering to the subject a first heat shock protein preparation;
- (b) administering to the subject an amount of a composition comprising activated antigen presenting cells, wherein the antigen presenting cells have been activated by contacting the antigen presenting cells with a second heat shock protein preparation; and
- (c) administering to the subject a vaccine composition comprising a component against which an immune response is desired to be induced, the vaccine composition being in an amount that is sub-immunogenic for the component in the absence of step(a)and/or step(c);

such that an immune response to the component is induced in the subject, and wherein the first and the second heat shock

protein preparations do not display the immunogenicity of the component.

75. A method of treating or preventing an infectious disease in a subject comprising the steps of:

- 5 (a) administering to the subject a vaccine composition comprising a component that displays the antigenicity of an infectious agent that causes the infectious disease;
- 10 (b) administering to the subject an amount of a first heat shock protein preparation effective in combination with step (a) and/or (c) to induce or increase an immune response to the component in the subject, wherein the first heat shock protein preparation does not display the immunogenicity of the component; and
- 15 (c) administering to the subject an amount of a composition comprising activated antigen presenting cells effective in combination with step (a) and/or (b) to induce or increase an immune response to the component in the subject, wherein the antigen presenting cells have been activated by contacting the antigen presenting cells with a second heat shock protein preparation which does not display the immunogenicity of the component;
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- 30 such that an immune response to the component is produced in the subject.

76. A method of treating or preventing a cancer in a subject comprising the steps of:

- 35 (a) administering to the subject a vaccine composition comprising a component that

displays the antigenicity of a cancer cell; and

(b) administering to the subject an amount of a first heat shock protein preparation effective in combination with step (a) and/or (c) to induce or increase an immune response in the subject to the component, wherein the first heat shock protein preparation does not display the immunogenicity of the component; and

(c) administering to the subject an amount of a composition comprising activated antigen presenting cells effective in combination with step (a) and/or (b) to induce or increase an immune response to the component in the subject, wherein the antigen presenting cells have been activated by contacting the antigen presenting cells with a second heat shock protein preparation which does not display the immunogenicity of the component;

such that an immune response to the component is produced in the subject.

77. The method according to claim 73, 74, 75, or 76 wherein the first heat shock protein preparation and the second heat shock protein preparation each comprises a heat shock protein selected from the group consisting of hsp70, hsp90, gp96, calreticulin, and a combination thereof.

78. The method according to claim 73, 74, 75, or 76 wherein the subject is human and the heat shock protein preparation comprises mammalian heat shock proteins.

79. A method for improving the outcome of a treatment using a therapeutic modality in a subject comprising administering to a subject receiving the



therapeutic modality a mammalian heat shock protein preparation, wherein the therapeutic modality is not a vaccine.

80. The method of claim 79 wherein the treatment modality is an antibiotic, an antiviral agent, an antifungal agent, a chemotherapeutic agent, or radiation.

81. The method of claim 79 wherein the subject is human and the heat shock protein preparation comprises human heat shock proteins.

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